REMARKS

Claims 1 to 38, as amended, appear in this application for the Examiner's review and consideration. Claims 8 to 28 have been withdraw from consideration. The amendments are fully supported by the specification and claims as originally filed. Other than the amendment of the preamble that adds the recitation that the presently claimed lansoprazole compound is a chemically stable lansoprazole compound, the present claims are substantially the same as the claims originally filed. Support for the recitation of a chemically stable lansoprazole compound is found throughout the specification. *See, e.g.*, page 3, lines 14 to 29, Table 1, page 13, and Table 2, page 16. Therefore, there is no issue of new matter. In addition, the amendments to the independent claims add recitations that elaborate on the structure of the presently claimed invention, and, thus, do not affect the scope of the claims. The amendments only further clarify the claimed invention.

Applicants wish to acknowledge with appreciation the courtesies shown to Applicants representative, Alan Force, Reg. No. 39,673, in telephone conferences with Examiner Morris on August 17, 2005, and April 3, 2006 ("the telephone interviews"). The arguments set forth herein are in accordance with those interviews.

The Amendment filed January 19, 2006, was allegedly not fully responsive to the Office Action dated July 19, 2005, for the reasons set forth on page 2 of the Office Action dated March 15, 2006. In particular, the March 15, 2006, Office Action stated:

> Applicants have now canceled the elected compounds. The original claims were drawn to compounds and pharmaceutical compositions containing the **compounds only**. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. See 37 C.F.R. 1.111 (emphasis in the original)

Moreover, in the April 3, 2006, interview, the Examiner stated that the election was to the compound lansoprazole only, and, as a result, it is Applicants understanding that the Examiner has apparently defined the claimed stable lansoprazole compound as chemically pure lansoprazole.

In response, Applicants submit that the original claims were clearly not directed to compounds only. Each of the claims, as originally filed, requires that the claimed stable lansoprazole compound further comprises at least a specified amount of water and/or a specified amount of alcohol. For example, claim 1, as originally filed, recites:

> 1. A stable lansoprazole compound, further comprising greater than 500 ppm and not more than about 3,000 ppm water.

Similarly, claim 3, as originally filed, recites:

> 3. A stable lansoprazole compound, further comprising greater than 200 ppm and not more than about 5,000 ppm alcohol.

Moreover, claim 5, as originally filed, recited,

> 5. A stable lansoprazole compound, further comprising greater than 500 ppm and not more than about 3,000 ppm water, and greater than 200 ppm and not more than about 5,000 ppm alcohol.

In addition to water and alcohol, the claims, as originally filed, also recite the presence of other impurities. For example, claim 6, as originally filed, recites:

> 6. The stable lansoprazole compound as in one of claims 1 to 5, further comprising less than about 0.1% (wt/wt) sulfone derivative and less than about 0.1% (wt/wt) sulfide derivative.

Therefore, the original claims were not drawn to the compounds only. That is the originally filed claims were not directed to a chemically pure lansoprazole compound. Instead, the originally filed claims were drawn to a stable lansoprazole compound comprising at least one impurity.

Moreover, one of ordinary skill in the art, in light of the present specification, would clearly understand that the present invention is directed to a stable lansoprazole that further comprises at least water and/or alcohol. For example, the present specification, at page 1, line 11 to 14, in the Field of the Invention section states

> The present invention relates to a stable 2-(2-pyridylmethyl) sulfinyl-1*H*-benzimidazole (lansoprazole) compound, further comprising either greater than 500 ppm and not more than about 3,000 ppm water, or greater than 200 ppm and not more than about 5,000 ppm alcohol or both.

Similarly, the Summary of the Invention, at page 3, line 32, to page 4, line 11, states

> The present invention provides a stable lansoprazole compound, further comprising greater than 500 ppm and not more than about 3,000 ppm water. Preferably, the stable lansoprazole compound comprises greater than about 600 ppm and not more than about 3,000 ppm water.
>
> The present invention provides a stable lansoprazole compound, further comprising greater than 200 ppm and not more than about 5,000 ppm alcohol. Preferably, the stable lansoprazole compound comprises greater than about 300 ppm and not more than about 5,000 ppm alcohol.
>
> The present invention provides a stable lansoprazole compound, further comprising greater than 500 ppm and not more than about 3,000 ppm water and greater than [ ] 200 ppm and not more than about 5,000 ppm alcohol.

The specification also clearly teaches that the stable lansoprazole compound of the invention may include other impurities in addition to water and alcohol. For example, at page 5, lines 17 to 19, in a disclosure of a process for purifying the lansoprazole compound of the invention, the specification states that

> the crystallized lansoprazole compound further comprises less than about 0.1% (wt/wt) sulfone derivative and less than about 0.1% sulfide derivative (wt/wt) sulfide derivative.

Similarly, at page 6, lines 11 to 19, the specification teaches:

> The present invention provides a lansoprazole substantially free of sulfone and sulfide (i.e., containing less than about 0.1% (wt/wt) sulfone derivative and less than about 0.1% (wt/wt) sulfide derivative). A "stable" lansoprazole refers to a lansoprazole that is stable (e.g., limited decomposition) under specified storage conditions (i.e., 2-8°C or 25°C at a relative humidity of up to 60% for a time period of up to about 6 months). In other words, a "stable" lansoprazole does not undergo discoloration and remains substantially free of sulfone and sulfide (i.e., containing less than about 0.1% (wt/wt) sulfone derivative and less than about 0.1% (wt/wt) sulfide derivative) under these specified storage conditions.

Other disclosures of possible impurities in lansoprazole can be found in the Examples, at pages 12 to 16 of the specification. Therefore, the specification and the claims, as originally filed, clearly teach that the stable lansoprazole compound of the presently claimed invention comprises lansoprazole and at least one of water and alcohol, and that the stable lansoprazole compound of the presently claimed invention may also comprise other impurities.

The Examiner has apparently elected to define the term "compound" in an extremely narrow manner. However, it is well settled law that Applicants can be their own lexicographers, as long as terms are not defined in manner that is repugnant to common usage. In the present case, in light of the specification and the originally filed claims, one of ordinary skill in the art will understand that Applicants have elected to define "lansoprazole compound" to mean lansoprazole containing one or more impurities. In this regard, one of ordinary skill in the art will understand that, other than in minute amounts, i.e., a few atoms or molecules, a sample of any compound comprises the compound and a number of ions, atoms, and/or molecules of impurities. It is extremely difficult, if not impossible, to remove all impurities from a bulk sample of a compound, even when the sample is as small as a few milligrams. Impurities in a compound will include those present in the environment, including gases, moisture, and particulates from the atmosphere and the environment, and reactants, solvents, and byproducts from the synthesis of the compound. Even where the compound is highly purified, impurities will be present. One millimole (0.001 mole) of a compound, having a purity of one part per trillion, will contain on the order of 6×10^8 atoms, ions, and/or molecules of impurities. One of ordinary skill in the art would clearly understand that no bulk sample of a compound is chemically pure, and, thus, free of any impurities. Therefore, the presently claimed invention and the claims, as originally filed, are not and were not directed to compounds only, as apparently defined by the Office Action dated March 15, 2006.

Moreover, the Restriction Requirement in the Office Action dated April 22, 2005, required election of one of the following inventions:

I. Claims 1 to 7 and 29 to 38, drawn to compounds;

II. Claims 8 to 22, drawn to multiple processes; and

III. Claims 23 to 28, drawn to a process.

If the Examiner's apparent definition of "compound" was correct, claims 1 to 7 and 29 to 38 would not have fallen into Group I. In particular, claims 1 to 7 are clearly directed to "compounds" that comprise lansoprazole and at least one of water and alcohol, and, thus, are not chemically pure compounds. Moreover, claims 29 to 38 are directed to pharmaceutical compositions, comprising the stable lansoprazole compound of the invention and a pharmaceutically acceptable excipient. Clearly, such pharmaceutical compositions, which comprise several elements, are not compounds, as apparently defined in the Office

Action. As stated above, the disclosure of the present application, the originally filed claims, and the present claims are all directed to a chemically stable lansoprazole compound that comprises specified ranges of impurities.

Therefore, the claims elected in response to the Restriction Requirement are not directed to compounds only, as apparently defined in the Office Action. Lansoprazole is a known compound, disclosed in U.S. Patent No. 4,628,098, as stated in the present specification at page 1, fourth paragraph. Instead, the present claims are directed to a chemically stable lansoprazole that can contains at least water and /or alcohol and, possibly, other impurities, but does not degrade chemically, producing additional impurities, as does prior art lansoprazole.

In response to the Office Action dated July 19, 2005, applicants amended the claims to change "lansoprazole compound" to --lansoprazole composition--. This amendment was made to demonstrate that the claims, as originally filed, were not directed to a chemically pure lansoprazole. However, as discussed above, that amendment was rejected in the current Office Action. In response, as discussed above, Applicants respectfully submit that one of ordinary skill in the art would understand the term "stable lansoprazole compound" in light of the specification to be lansoprazole containing one or more impurities. Accordingly, applicants have amended the claims to again recite a lansoprazole compound.

Therefore, Applicants submit that the Amendment filed January 19, 2006, is fully responsive to the Office Action dated July 19, 2005. Accordingly, it is respectfully requested that the Examiner consider the arguments set forth below, addressing the rejections set forth in the July 19, 2005, Office Action.

Should the Examiner not agree with Applicants position an interview with the Examiner and her supervisor is respectfully requested.

In the Office Action dated July 15, 2005, claims 1 to 7 and 29 to 38 were rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement, for the reasons set forth on pages 4 to 8 of that Office Action.

In particular, the rejection is based on the possibility of a change in polymorphic state of a crystalline form of a compound during storage or tablet preparation. The Office Action, at page 5, states

> The specification lacks description of how the pharmaceutical composition can be prepared in order to maintain the particular compound of a particular form with the particular infrared and x-ray diffraction being claimed.

> Disclosure of x-ray diffraction patterns for the compounds and pharmaceutical compositions comprising the polymorphic forms are lacking in the specification. The specification has also not described how the stable form and composition's being claimed will be maintained and prevented from converting to other forms.

In response, Applicants respectfully submit that XRD and IR spectra are not provided, and there is no teaching in the specification on how to maintain a particular polymorphic form, because a new polymorphic crystalline form of lansoprazole is not disclosed or claimed in the present application. The presently claimed invention is directed to a chemically stable lansoprazole compound. That is, the presently claimed invention is a chemically stable lansoprazole compound, which may be first produced in a known process, but has been chemically stabilized with the method of the invention. The present claims are not directed to a new polymorphic crystalline form, and, thus, no XRD or IR spectral data are required. No disclosure of how to prevent the chemically stable lansoprazole of the invention from converting to a different polymorphic form is provided, because the invention is not directed to a polymorphic form.

At pages 1 to 3, the present specification discusses the instability of prior art lansoprazole. As will be understood by one of ordinary skill in the art, the instability of lansoprazole discussed in the specification is not a polymorphic instability. Instead, the instability discussed in the specification is a chemical instability. When prior art lansoprazole is stored or exposed to heat and humidity, a chemical change occurs, producing impurities in the form of different chemical compounds. At page 3, lines 2 to 12, the present specification states that during storage, prior art lansoprazole degrades, such that the concentration of lansoprazole decreases, resulting in discoloration. Degradation of a compound results from a chemical change, not a change in polymorphic form, as alleged in the Office Action.

Moreover, the present specification clearly teaches one of ordinary skill in the art how to make and use the invention, and the specification describes the claimed subject matter in such a way as to reasonably covey to one skilled in the relevant art that the Applicants had possession of the claimed invention at the time the application was filed.

In the first paragraph of the Detailed Description on page 7, the specification discloses the impurities that are formed in lansoprazole during storage. The impurities are further disclosed in Tables 1 and 2 on pages 13 and 16 of the specification, respectively. Processes for preparing the presently claimed chemically stable lansoprazole are set forth in both the

Summary and Detailed Description sections of the specification, and are particularly exemplified in Examples 2 and 3 on pages 12 to 14 of the specification. The superior chemical stability of the presently claimed chemically stable lansoprazole, compared to prior art lansoprazole, is set forth in the aforementioned Tables 1 and 2.

Clearly, one of ordinary skill in the art would understand how to make and use the presently claimed invention from the present specification.

With respect to an alleged lack of description as to whether the pharmaceutical carriers are able to maintain the presently claimed chemically stable lansoprazole in the stable form claimed, one of ordinary skill in the art, from the present specification, would understand how to make and use the presently claimed pharmaceutical compositions. Pharmaceutical carriers, diluents, disintegrates, binders, giants, dyes, colorants, lubricants, excipients, and the like, useful in the invention, are set forth on pages 9 to 12.

Therefore, as the presently claimed invention is not directed to stable polymorphs, but, instead, is directed to a chemically stable lansoprazole compound, the present specification clearly teaches one of ordinary skill in the art how to make and use the claimed invention, and, thus, the claims meet the requirements of 35 U.S.C. §112, first paragraph. Accordingly, it is respectfully requested that the Examiner withdraw the rejection of claims 1 to 7 and 29 to 38 under 35 U.S.C. § 112, first paragraph.

Claims 1 to 7 and 29 to 38 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for the reasons set forth on pages 8 and 9 of the Office Action. In particular, the Office Action stated that the expressions "comprising" and "further comprising" are open ended, allowing the inclusion of other parameters allegedly not contemplated by Applicants. During the telephone interviews, the Examiner stated that the present claims were directed to a compound, and, thus, could not be open ended. Applicants understand this to mean that a compound has a specific structure that cannot be modified without changing the compound to a different compound, and that, as discussed above, must be chemically pure.

In response, Applicants submit that, as discussed above, one of ordinary skill in the art would understand the presently claimed invention in light of the claims and specification, as originally filed, to be directed to a chemically stable lansoprazole that comprises one or more impurities in the amounts specified in the claims. As the originally filed claims clearly recite that the claimed lansoprazole compound comprises or further comprises certain

impurities in specified amounts, and lansoprazole compounds comprising those impurities are clearly disclosed in the specification, as filed, lansoprazole compounds comprising such impurities were clearly contemplated by Applicants. Moreover, as discussed above, one of ordinary skill in the art would clearly understand that a bulk sample of any chemical compound comprises impurities, such as those introduced from the environment, and those introduced or formed in the synthesis of the compound. Again, at the time the application was filed, Applicants clearly contemplated the inclusion of various impurities in the lansoprazole compounds of the invention.

To better clarify the presently claimed invention, in light of the prior art rejections discussed below, Applicants have amended the claims to recite a chemically stable lansoprazole compound, and submit that one of ordinary skill in the art would understand that it is virtually impossible for any given sample of lansoprazole to be 100 percent pure lansoprazole. Instead, a sample of lansoprazole contains lansoprazole and trace amounts of water and/or alcohol, as well as trace amounts of other impurities, and, thus, is effectively a lansoprazole composition, even where the lansoprazole is of a very high purity. Even with the presently claimed stable lansoprazole compound, it is practically impossible to remove all impurities, although the rate at which the amount of any impurities in the presently claimed stable lansoprazole composition increases is significantly slower during storage than the rate at which impurities are formed in prior art lansoprazole. Thus, one of ordinary skill in the art would understand that the "stable lansoprazole compound" of the present invention, as recited in the originally filed claims, is actually a chemically stable lansoprazole compound that contains trace amounts of impurities, such as the water and alcohol recited in claims 1, 3, and 5 and the sulfone and sulfide derivatives recited in claim 6. It would also be understood by one of ordinary skill in the art that any bulk sample of lansoprazole would most likely also contain at least trace amounts of impurities other than those recited in the claims. Accordingly, Applicants did contemplate the inclusion of other parameters not recited in the claims. Thus, the present claims are open ended, but still meet the requirements of 35 U.S.C. § 112. As noted above, one of ordinary skill in the art would understand that the originally claimed "stable lansoprazole compound" was a composition comprising lansoprazole, water and/or alcohol, and other trace impurities, and, thus, the presently claimed stable lansoprazole composition is fully supported by the application and claims, as originally filed.

With regard to the recitation of sulfone derivative and sulfide derivative in claims 6 and 34, those terms would be understood by one of ordinary skill in the art in light of the specification and knowledge in the art. For example, in the first full paragraph of page 2, the specification states that preparation of lansoprazole by conventional methods is always accompanied by the formation of small quantities of the corresponding sulfone derivative and an impurity, and that U.S. Patent No. 6,180,652 describes the presence of the sulfone derivative in lansoprazole. Moreover, the sulfide derivative is identified as LNPS in the Detailed Description of the Invention, at page 6, lines 7 to 9. The sulfone derivative and sulfide derivatives are also clearly defined in Tables 1 and 2 on pages 13 and 16 of the specification, respectively, and, thus, would be understood by one of ordinary skill in the art. As the terms "sulfone derivative" and "sulfide derivative" would be understood by one of ordinary skill in the art in light of the specification, those terms are not indefinite under 35 U.S.C. § 112, second paragraph.

With regard to the alleged lack of antecedent basis for the limitations recited in claims 2 to 7 and 30 to 38, M.P.E.P. § 2173.05(e) states:

> A claim is indefinite when it contains words or phrases whose meaning is unclear. The lack of clarity could arise where a claim refers to "said lever" or "the lever," where the claim contains no earlier recitation or limitation of a lever and where it would be unclear as to what element the limitation was making reference. Similarly, if two different levers are recited earlier in the claim, the recitation of "said lever" in the same or subsequent claim would be unclear where it is uncertain which of the two levers was intended. A claim which refers to "said aluminum lever," but recites only "a lever" earlier in the claim, is indefinite because it is uncertain as to the lever to which reference is made. Obviously, however, the failure to provide explicit antecedent basis for terms does not always render a claim indefinite. If the scope of a claim would be reasonably ascertainable by those skilled in the art, then the claim is not indefinite. *Ex parte Porter*, 25 USPQ2d 1144, 1145 (Bd. Pat. App. & Inter. 1992) ("controlled stream of fluid" provided reasonable antecedent basis for "the controlled fluid"). Inherent components of elements recited have antecedent basis in the recitation of the components themselves. For example, the limitation "the outer surface of said sphere" would not require an antecedent recitation that the sphere has an outer surface. >*See Bose Corp. v. JBL, Inc.*, 274 F.3d 1354, 1359, 61 USPQ2d 1216, 1218-19 (Fed. Cir 2001) (holding that recitation of "an ellipse" provided antecedent basis for "an ellipse having a major diameter" because "[t]here can be no dispute that mathematically an inherent characteristic of an ellipse is a major diameter").

Applicants submit that it is not unclear as to which elements of the invention the limitations of the claims make reference, as, where necessary, the proper antecedent basis is provided in the claims. There is no initial reference in any of the claims to "the water," "the alcohol," "the sulfone derivative," "the sulfide derivative," or "the lansoprazole" in any of the claims, such that it would be unclear as to what element the limitation was making reference. All of the present claims and the claims, as originally filed are in proper form, and provide the required antecedent basis for all of the claimed elements.

In this regard, one of ordinary skill in the art would understand that the presently claimed lansoprazole compounds comprise water and/or alcohol. For example, independent claim 1 is directed to a chemically stable lansoprazole compound, comprising greater than 500 ppm and not more than about 3,000 ppm water. That is, claim 1 recites a lansoprazole compound in which water is present in an amount greater than 500 ppm and not more than about 3,000 ppm. This provides the necessary antecedent basis for the recitation of lansoprazole and water in claim 2, which depends from claim 1.

Independent claim 3 is directed to a stable lansoprazole compound, comprising greater than 200 ppm and not more than about 5,000 ppm alcohol. That is, independent claim 3 recites a stable lansoprazole compound in which alcohol is present in an amount greater than 200 ppm and not more than about 5,000 ppm. As claim 3 is independent, it does not depend from or refer back to an earlier claim. The recitation of alcohol in that independent claim is not a recitation to earlier referenced limitations, but, instead, is a recitation of the elements of the claimed composition. No antecedent basis is required. This recitation also provides the necessary antecedent basis for the recitation of alcohol in claim 4, which depends from claim 3.

Independent claim 5 is directed to a stable lansoprazole compound, comprising chemically stable lansoprazole and greater than 500 ppm and not more than about 3,000 ppm water, and greater than 200 ppm and not more than about 5,000 ppm alcohol. That is, independent claim 5 recites a stable lansoprazole compound, comprising water and alcohol, in which the water is present in an amount greater than 500 ppm and not more than about 3,000 ppm, and the alcohol is present in an amount greater than 200 ppm and not more than about 5,000. As claim 5 is independent, it does not depend from or refer back to an earlier claim. The recitation of water and alcohol in that independent claim is not a recitation to

earlier referenced limitations, but, instead, is a recitation of the elements of the claimed composition. No antecedent basis is required.

Claim 6 is directed to the stable lansoprazole composition of any of claims 1 to 5, which further comprises less than about 0.1% (wt/wt) sulfone derivative and less than about 0.1% (wt/wt) sulfide derivative. The recitation of the sulfone and sulfide derivatives in claim 6 is not a recitation to earlier referenced limitations, but, instead, is an initial recitation of possible additional elements of the claimed composition, and sets a maximum for the amounts of the recited elements. Claim 6 does not recite "the sulfone derivative" or "the sulfide derivative," and, thus, no additional antecedent basis is required.

Claim 7 is directed to the stable lansoprazole compound of any of claims 1 to 5, where the lansoprazole compound is stable at a temperature of from 2° to 8°C or 25°C at a relative humidity of up to 60% for a time period of up to about 6 months. The recitation in claim 7 of the temperature and humidity conditions to which the claimed lansoprazole is subjected is not a recitation to earlier referenced limitations, but, instead, is an initial recitation of the stability of the claimed composition. As the claim does not refer back to the recitation of stability conditions in prior claims, no additional antecedent basis is required.

Similarly, with regard to claims 30 to 38, one of ordinary skill in the art would understand that those claims are directed to pharmaceutical compositions, comprising a chemically stable lansoprazole, an excipient, and water and/or alcohol. Claim 34, as with claim 6, recites possible additional elements of the claimed composition, and sets a maximum amount for each of the additional elements. Claims 35 to 38 recite dosage forms and dosage levels for the claimed chemically stable lansoprazole. No additional antecedent basis is required for the elements of any of those claims.

Moreover, all of the claimed elements of the inventions and the amounts recited in the claims are fully supported in the specification. Therefore, there is no lack of an antecedent basis in any of the claims.

With regard to the alleged failure of claims 29 to 38 to recite the presence of an inert carrier in the composition, claims 29, 31, and 33 each recite that the claimed pharmaceutical compositions comprises a pharmaceutically acceptable excipient. By definition, an excipient is a substance used as a diluent or carrier for a drug. Therefore, the claims are directed to compositions comprising a carrier.

Therefore, the claims particularly point out and distinctly claim the subject matter Applicants regard as the invention, and, thus, the claims are not indefinite. Accordingly, it is respectfully requested that the Examiner withdraw the rejection of claims 1 to 7 and 29 to 38 under 35 U.S.C. §112, second paragraph.

In the Office Action dated July 15, 2005, claims 1 to 7 and 29 to 38 were rejected under 35 U.S.C. §102(a), (b), and/or (e), as allegedly being anticipated by Vrečer et al., Farmacevtski Vestnik (Ljubljana) 1997, 48, pages 242 and 243 (Vrečer), Kotar et al., Eur. J. Pharm. Sci, 1996, 4, page S182 (Kotar), WO 01/21617 to Choi et al., (Choi), U.S. Patent No. 4,628,098 to Nohara et al. (Nohara), U.S. Patent Application Publication No. 2004/0192923 to Singer et al. (Singer), U.S. Patent No. 6,002,011 to Kato et al. (Kato), and U.S. Patent Application Publications Nos. 2003/0036554 and 2004/0138466 to Avrutov et al. (Avrutov I and Avrutov II, respectively, and, collectively, Avrutov)) for the reasons set forth on pages 2 and 3 of the Office Action, and under 35 U.S.C. §103(a) as being unpatentable over the combined teachings of Vrečer, Kotar, Choi, Nohara, Singer, Kato, and Avrutov in view of Hableblian et al., J. of Pharmaceutical Sciences, 1964, 58, pages 911-929 (Hableblian). Chemical & Engineering News, Feb. 2003, (C&E News), U.S. Pharmacopia, 1995, pp 1843-1844, Muzaffar et al., J. of Pharmacy (Lahore) 1979, 1(1), 59-66, (Muzaffar), Jain et al., Indian Drugs, 1986, 23(6), pages 315-329, (Jain), Taday et al., J. of Pharm. Sci., 92(4), April 2003, 831-838, (Taday), and Concise Encyclopedia Chemistry, page 872-873 (1993), for the reasons set forth on pages 3 and 4 of the Office Action.

In response, Applicants submit that, as recited in claim 1, the presently claimed invention is directed to a chemically stable lansoprazole compound, further comprising greater than 500 ppm and not more than about 3,000 ppm water; as recited in claim 3, the presently claimed invention is directed to a chemically stable lansoprazole compound, further comprising greater than 200 ppm and not more than about 5,000 ppm alcohol; and, as recited in claim 5, the presently claimed invention is directed to a chemically stable lansoprazole compound, further comprising greater than 500 ppm and not more than about 3,000 ppm water, and greater than 200 ppm and not more than about 5,000 ppm alcohol. Applicants also submit that, as recited in claim 29 to 38, the presently claimed invention is directed to pharmaceutical compositions, comprising the chemically stable lansoprazole compositions of claims 1, 3, and/or 5 and a pharmaceutically acceptable excipient.

As demonstrated by Examples 2 and 3 and Table 2 of the present specification, the presently claimed chemically stable lansoprazole compound is substantially more chemically stable than prior art lansoprazole. After three months at 40°C and a relative humidity of 75 percent, the stable lansoprazole composition of the invention contains only 0.02 percent of the sulfide compound and 0.03 percent of the sulfone compound, and remains white. In contrast, under the same conditions, the non-stabilized, prior art lansoprazole contains 0.04 percent of the sulfide compound and 0.06 percent of the sulfone compound, and has changed color. Present specification, Examples 2 and 3, pages 12 to 16, and Table 2, page 16.

Although the cited prior art references may disclose lansoprazole and polymorphs of lansoprazole, the references disclose non-stable, prior art lansoprazole, and do not disclose or suggest the presently claimed chemically stable lansoprazole.

In contrast to the presently claimed invention, Vrečer discloses the relative physical stability of polymorphic forms A and B of prior art lansoprazole. In particular, Vrečer discloses that lansoprazole polymorphic form B is not physically stable, and transforms to polymorphic form A on heating. Vrečer discloses only non-stable, prior art lansoprazole, and, thus, Vrečer does not disclose or suggest a chemically stable lansoprazole, as presently claimed.

Similarly, Kotar discloses the analysis of polymorphs of prior art lansoprazole, and that lansoprazole form B is not stable, undergoing a solid-solid transition to form A. Kotar discloses only non-stable, prior art lansoprazole, and, thus, Kotar does not disclose or suggest the presently claimed chemically stable lansoprazole.

Choi discloses a process for preparing conventional prior art sulfoxide compounds, such as lansoprazole, comprising oxidizing a sulfide compound with hydrogen peroxide in the presence of a rhenium catalyst. The disclosed process reportedly minimizes the production of N-oxide and sulfone byproducts. Page 1, lines 4 to 17. The m-chloroperbenzoic acid, used in the prior art as the oxidizing agent, reportedly results in the formation of the N-oxide and sulfone byproducts, resulting in a low yield in the preparation. Page 3, lines 9 to 22. Other prior art processes, such as the oxidation of the sulfide compound with hydrogen peroxide in the presence of a vanadium catalyst, reportedly result in the production of more than 1 HPLC area percent of the sulfone compound and a product containing 0.4 percent of that compound after purification. Page 6, lines 2 to 9, and page 7,

lines 1 to 11. The disclosed process reportedly minimizes the production of the N-oxide and sulfone by products, and removes the by products by filtration.

The lansoprazole disclosed by Choi is a non-stable, prior art lansoprazole, and, thus, Choi does not disclose or suggest the chemically stable lansoprazole of the presently claimed invention.

Nohara discloses 2-[2 pyridylmethylthio-(sulfinyl)-] benzinidazoles and processes for preparing such compounds. A sulfide derivative, prepared with the disclosed process, can be oxidized to prepare a sulfinyl derivative. Column 2, lines 21 to 48. Compounds produced with the disclosed process "can be isolated and purified by conventional means, e.g., crystallization and chromatography." Column 2, lines 66 to 68.

Nohara discloses only non-stable, prior art lansoprazole, and, thus, does not disclose or suggest the presently claimed chemically stable lansoprazole.

With regard to Singer, Applicants submit that that application is not prior art to the present claims. The Applicants of the present application are named inventors of Singer, and have assigned their rights to both applications to the same assignee. As evidence of Applicants' position, Applicants have previously submitted a Declaration under 37 C.F.R. §1.131 with the required supporting documentation.

Kato discloses a prior art substantially solvent-free lansoprazole that is free of decomposition in the course of vacuum drying. Column 2, lines 22 to 26. Kato specifically teaches that

> It is understood that the water content of the substantially solvent-free crystals according to the present invention is not higher than about 500 ppm, preferably not higher than about 300 ppm, and, for still better results, not higher than about 200 ppm, and the alcohol (e.g. ethanol) content is not higher than about 200 ppm, preferably not higher about 100 ppm, and, for still better results, not higher about 80 ppm. Column 7, lines 24 to 30.

Therefore, Kato does not disclose or suggest a stable lansoprazole composition, comprising chemically stable lansoprazole and greater than 500 ppm and not more than about 3,000 ppm water and/or greater than 200 ppm and not more than about 5,000 ppm alcohol, as presently claimed. Moreover, by teaching that the disclosed lansoprazole must contain less than 500 ppm of water and 200 ppm of alcohol, Kato teaches away from the presently claimed invention.

Avrutov discloses processes for preparing substituted 2-(2-pyridylmethyl)sulfinyl-1-H-benzimidizoles. Avrutov I and II, page 1, paragraph [0002]. In particular, Avrutov discloses a selective oxidation process for preparing lansoprazole. Avrutov I, page 2, paragraph [0016]; Avrutov II, page 2, paragraph [0025].

Avrutov discloses only non-stable, prior art lansoprazole. Therefore, Avrutov does not disclose or suggest the presently claimed invention.

The other cited references do nothing to overcome the deficiencies of Vrečer, Kotar, Choi, Nohara, Singer, Kato, and Avrutov. As stated at page 4 of the Office Action, Hableblian, Muzaffar, Jain, and Taday each teach that some crystalline compounds can exist in different crystalline forms. The Office Action also states, at page 4, that C & E News, Muzaffar, U.S. Pharmacopia, and Concise Encyclopedia of Chemistry all teach that, at any particular temperature and pressure, only one crystalline form is thermodynamically stable.

However, as discussed above, the presently claimed invention is directed to a chemically stable lansoprazole, not a thermodynamically stable polymorphic form. None of the cited references whether taken alone or in combination, disclose or suggest the presently claimed chemically stable lansoprazole. Instead, the cited prior art references discloses only non-stable, prior art lansoprazole.

Therefore, as the cited references, whether taken alone or in combination do not disclose or suggest the presently claimed invention, the claims are not anticipated by or obvious over the cited references. Accordingly, it is respectfully requested that the Examiner withdraw the rejections of claims 1 to 7 and 29 to 38 under 35 U.S.C. §§ 102 (a), (b), and/or (e) and 103(a).

Applicants thus submit that the entire application is now in condition for allowance, an early notice of which would be appreciated. Should the Examiner not agree with Applicants' position, a personal or telephonic interview with the Examiner and the Examiner's supervisor is respectfully requested to discuss any remaining issues prior to the issuance of a further Office Action, and to expedite the allowance of the application.

A separate Petition for an Extension-of-Time is submitted herewith. Should any other fees be due, however, please charge such fees to Deposit Account No. 11-0600.

Respectfully submitted,

KENYON & KENYON LLP

Dated: September 14, 2006

By: 

Alan P. Force
Reg. No. 39,673
One Broadway
New York, NY 10004
(212) 425-7200